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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	9

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/214,913	SMITH ET AL	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/16/99; 09/13/00* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32, 34-37, 39, 41-45, 47-48, 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-32, 34-37, 39, 41-45, 47-48, 50-52* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d)

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

15☐ Notice of References Cited (PTO-892)

16☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

16☐ Interview Summary (PTO-413) Paper No.s

19☐ Notice of Informal Patent Application (PTO-152)

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Group 1640, Technology Center 1600.

2. The instant application is in sequence compliance for patent applications containing amino acid sequence disclosures.
However, Applicant is reminded to amend the claims to indicate SEQ. ID NOS.

3. **Please Note**: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

4. Applicant's preliminary Amendment (Paper No. 4), filed on 3/16/99, and Amendment B (Paper No. 7), filed on 9/13/00 are acknowledged.
Claims 33, 38, 40, 46 and 49 have been canceled.
Claims 4-8, 10, 12-14, 16, 19, 22-23, 27, 29, 34-35, 37, 39, 41-42, 44-45, and 47-48 have been amended.
Claims 50-52 have been added.
Claims 1-32, 34-37, 39, 41-45, 47-48, 50-52 are pending.

Election/Restrictions

5. The following is noted:

Independent claim 1, and dependent claims thereof encompass a fusion polypeptide containing a cell specific soluble polypeptide and a membrane specific binding element wherein the soluble polypeptide as recited in claims 8, 23, 18 is:

A) IL-4 Y124D mutein (B cell specific).

B) Prourokinase.

C) Streptokinase.

D) Tissue-type plasminogen activator.

E) Reteplase.

F) Leptin.

G) Complement inhibitors from complement regulatory proteins, hydrids and muteins thereof

H) scFv antibody against cytokines.

I) Protein Kinase C.

J) Antibodies against CD4.

K) Antibodies against B7/CD28.

L) Antibodies against CD3/TCR.

M) Antibodies against CD11b (CR3).

N) Interferon-β and derivatives.

O) CR1 polypeptide fragment, or

P) Thrombolytic agent, or

Q) Rabbit anti-human erythrocyte membrane antibody.

Wherein the membrane binding element as recited in claims 8-11 is:

A) Fatty acid derivative from aliphatic acyl groups with about 8 to 18 methylene units.

B) Fatty acid derivative from long-chain (8 to 18 methylene) aliphatic amines and thiols.

C) Steroid.

D) Farnesyl derivatives.

F) Basic amino acid sequence from DGPKKKKKKSPSKSSG.

G) [illegible] GSSKSPSKKKKKKPGD

[illegible] DGPKKKKKKSPSKSSK

J) Basic amino acid sequence from SKDGKKKKKKSKTK.

K) Integral membrane protein from GRGDSP.

L) Integral membrane protein from DGPSEILRGDFSS.

M) Integral membrane protein from GNEQSFRVDLRTLLRYA.

N) Integral membrane protein from GFRILLLKV.

O) Integral membrane protein from SAAPSSGFRILLLKV.

P) Integral membrane protein from AAPSVIGFRILLLKVAG or

Q) The carbohydrate ligand Sialyl Lewis^{x}.

These fusion proteins are unique products. They differ with respect to their structures, molecular composition, target specificity and mode of action; a person of ordinary skill in the art would not envision one in view of the other. Therefore, the restriction has been set forth for each as separate groups, irrespective of the format of the claims.

6. Restriction to one of the following inventions is required under 35 U.S.C. 121 and 372:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this Office Action, to elect a single invention to which the claims must be restricted:

I. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a fatty acid derivative from aliphatic acyl group about 1-18 methylene unit, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

II Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a fatty acid derivative from long-chain (8-18 methylene) aliphatic amines and thiols, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

III. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a fatty acid derivative from steroid, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

IV. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a fatty acid derivative from farnesyl derivatives, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

V. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a basic amino acid sequence consisting of DGPKKKKKKSPSKSSG, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

VI. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a basic amino acid sequence consisting of GSSKSPSKKKKKPGD, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

VII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a basic amino acid sequence consisting of SPSNETPKKKKKRFSFKKSG, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

VIII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a basic amino acid sequence consisting of DGPKKKKKKSPSKSSK, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

IX. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a basic amino acid sequence consisting of SKDGKKKKKKSKTK, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

X. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble

XI. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of DGPSEILRGDFSS, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of GNEQSFRVDLRTLLRYA, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XIII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of GFRILLLKV, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

IX. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of SAAPSSGFRILLLKV, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

X. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of AAPSVIGFRILLLKVAG, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XI Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is a ligand of known integral membrane proteins consisting of the carbohydrate ligand Sialyl Lewis, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is IL-4 Y124D mutein, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XIII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is prourokinase, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XIV. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is streptokinase, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XV. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is tissue-type plasminogen activator, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XVI. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is reteplase, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XVII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is leptin, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XVIII Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is complement inhibitor from complement regulatory proteins and hybrids, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350

XIX. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble

XX. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against Protein C, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXI. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against CD4, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against B7/CD28, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXIII. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against CD3/TCR, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXIV. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against CD11b(CR3), and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXV. Claims 1-24, 26-28, 35-37, 41, 44, 47 and 50, drawn to soluble derivative of a soluble polypeptide derivative with membrane binding elements wherein the membrane binding element is sc Fv antibody against interferon-β and derivatives, and pharmaceutical composition of said polypeptide classified in Class 530, subclass 350.

XXVII Claims 25, 29-31, drawn to a process for preparing a derivative which comprises DNA encoding polypeptide, vector, host cells, and DNA encoding polypeptides classified in Class 526, subclass 23.1; Class 536, subclass 24.1, and Class 435, subclass 252.3.

XXVIII. Claims 32, 34, and 52 drawn to peptide membrane binding elements, classified in class 530, subclass 300.

XXIX. [illegible]

XXX. Claim 42-43, drawn to a method of treating a disease or disorder associated with inflammation or inappropriate complement activation using a soluble complement inhibitor, classified in Class 435, subclass 69.1.

XXXI. Claim 45, drawn to a method of treating a disease or disorder associated with inflammation or inappropriate complement activation using a soluble CR1 polypeptide derivative, classified in Class 435, subclass 69.1.

XXXII. Claim 48 and 51 drawn to a method of treating thrombotic disorders with a derivative of thrombolytic agent, classified in Class 435, subclass 69.1.

The inventions listed as Groups I-VII above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Hebell *et al.* teach soluble derivative of a soluble polypeptide comprising heterologous membrane binding elements of complement receptor type 1 (CR1) derivatives for treating disease or disorders associated with inflammation, and inappropriate complement activation (Claims 1, 13, 19, 20, 37, 39, see entire document, in particular, page 4, 3rd paragraph – page 5, 2nd paragraph).

Marsh *et al.* teach treatment of neurological disorder, inappropriate complement activation, inflammatory disorder, and thrombotic disorders using soluble complement and thrombolytic agent (Claim 23, See entire document, in particular page 6-7).

Since Applicant's Inventions do not contribute a special technical feature when viewed over the prior art, they do not have a single general inventive concept and lack unity of invention.

7. This application contains claims directed to the following distinct species of the claimed Inventions of Groups IV-VII as disclosed in the specification on page 23-24 wherein the neurological disease or disorder involving complement is:

A) Multiple sclerosis,

B) Stroke,

C) Guillain Barre Syndrome,

D) [illegible]

G) Alzheimer's disease.

Wherein disorder of Inappropriate Complement Activation is:

A) Heamodialysis complications,

B) Hyperacute allograft rejection,

C) Xenograft rejection,

D) Corneal graft rejection,

E) Interleukin-2 induced toxicity during IL-2 therapy, or

F) Paroxysmal nocturnal haemoglobinuria.

Wherein inflammatory disorder is:

A) Crohn's disease,

B) Adult respiratory distress syndrome,

C) Thermal injury including burns or frostbite,

D) Uveitis,

E) Psoriasis,

F) Asthma, or

G) Acute pancreatitis.

Wherein Post-Ischemic Reperfusion Condition is:

A) Myocardial infarction,

B) Balloon angioplasty,

C) Atherosclerosis (cholesterol-induced) and restenosis,

D) Hypertension,

E) Post-pump syndrome in Cardiopulmonary bypass or renal haemodialysis,

F) Renal ischemia, or

G) Intestinal ischemia.

These species are distinct because the specific diseases differ with respect to their

To elect a specific disease or disorders as recited in claims 39, 42, 45 and 48, to be treated if Group XXIX, Group XXX, Group XXXI, or Group XXXII is elected.

8. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 8, 9, 11, 12, 13, 15, 16, 17, 21, 22, 24, 34 are generic.

9. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

11. A telephone call to request an oral election was not made due to the complexity of the restriction.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

13 Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
December 11, 2000

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
12/14/00